



IN THE CLAIMS:

Please cancel claims 1 to 10, 12, 13, 15 to 19, 32, 43 to 45, 48, 49 and 52, without prejudice.

11. (amended) A DNA delivery system comprising DNA in association with a carrier, said DNA coding for a recombinant chimeric receptor capable of ~~one~~ type of extracellular interaction [and comprising two or more different cytoplasmic signalling components which are not naturally linked, and wherein at least one of said cytoplasmic components is derived from a membrane spanning polypeptide] and wherein said DNA codes in reading frame for:

- i) a signal peptide component;
- ii) an antibody or antigen binding fragment thereof;
- iii) a transmembrane component;
- iv) two or more different cytoplasmic signalling components which are not naturally linked, and wherein at least one of said cytoplasmic components is derived from a membrane spanning polypeptide; and optionally
- v) one or more spacer regions linking any two or more of said i) to iv) components.

14. (amended) A DNA delivery system according to Claim 11 wherein said DNA comprises

- 1) a first DNA which codes in reading frame for:
 - i) a signal peptide component;
 - ii) [part of a binding component;] a first chain of an antibody or an antigen binding fragment thereof;
 - iii) a transmembrane component;
 - iv) two or more cytoplasmic signalling components which are not naturally linked, and wherein at least one of said cytoplasmic components is derived from a membrane spanning polypeptide: and [optionally
 - v) One or more spacer regions linking any two or more of said i) to iv) components; and]

13 2) a second separate DNA which codes in reading frame for a signal peptide component and [a further part of the binding component ii) coded for by said first DNA, such that the binding component parts together are] a second chain of an antibody or an antigen binding fragment thereof such that upon co-expression of said first and second DNA sequences, said first and second chains of an antibody or antigen binding fragment thereof assemble to form a binding component capable of [recognising] recognizing a cell surface molecule on a target cell.

20. (amended) [A] The DNA delivery system according to Claim [19] 11 wherein the antibody or fragment thereof is an engineered human antibody or antigen binding fragment thereof.

22 21. (amended) [A] The DNA delivery system according to [Claims 18 to 20] claim 11 wherein the binding component is a single chain Fv fragment.

22. (amended) [A] The DNA delivery system according to [Claims 18 and 20] claim 11 wherein the binding component is a Fab' fragment.

23. (amended) [A] The DNA delivery system according to [any one of Claims 13 to 22] claim 11 wherein the transmembrane component is derived from all or part of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD8, CD4, a cytokine receptor or a colony stimulating factor receptor.

24. (amended) [A] The DNA delivery system according to Claim 23 wherein the transmembrane component is derived from all or part of CD28.

25. (amended) [A] The DNA delivery system according to [any one of] Claim 11 [to 24] wherein the cytoplasmic signalling components are capable of acting together cooperatively.

26. (amended) [A] The DNA delivery system according to [any one of Claim 13 to 25] claim 11 wherein the cytoplasmic signalling components are derived from all

or part of the cytoplasmic domains of a zeta, eta or epsilon chain of the T-cell receptor, CD28, the 7 chain of a Fc receptor, a cytokine receptor, a colony stimulating factor receptor, a tyrosine kinase or an adhesion molecule, B29, MB-1, CD3 delta, CD3 gamma, CD5 or CD2.

27. (amended) [A] The DNA delivery system according to Claim [26] 11 wherein the cytoplasmic signalling components are ITAM containing cytoplasmic components.

28. (amended) [A] The DNA delivery system according to Claim 26 [or Claim 27] wherein the cytoplasmic signalling components are derived from all or part of CD28 [and/or] or the zeta chain of the T-cell receptor.

29. (amended) [A] The DNA delivery system according to [any one of Claims 11 to 28] claim 11 wherein the cytoplasmic signalling components are in any orientation relative to one another.

30. (amended) [A] The DNA delivery system according to [any one of Claims 13 to 29] claim 11 wherein said DNA coding for components i) to iv) additionally codes for one or more spacer regions linking the [binding component] antibody or antigen binding fragment thereof ii) and the transmembrane component iii).

31. (amended) [A] The DNA delivery system according to [Claim 30] claim 11 wherein two or more different spacer regions link the binding component ii) and the transmembrane component iii), both regions either being coded for by one DNA sequence or when a first and second DNA sequence is present one region being coded for by said first DNA and the other different region being coded for by said second DNA.

33. (amended) [A] The DNA delivery system according to [Claims 30 to 32] claim 11 wherein the spacer region is derived from all or part of the extracellular region of CD8, CD4 or CD28.

34. (amended) [A] The DNA delivery system according to [Claims 30 or Claim 32] claim 11 wherein the spacer region is all or part of an antibody constant region.

35. (amended) [A] The DNA delivery system according to [Claims 30 to 32] claim 11 wherein the spacer region is derived from all or part of an antibody hinge region linked to all or part of the extracellular region of CD28.

36. (amended) [A] The DNA delivery system according to [any one of Claims 11 to 35] claim 11 wherein the carrier is a viral vector or a non-viral vector.

37. (amended) [A] The DNA delivery system according to Claim 36 wherein the non-viral vector is a liposomal vector.

38. (amended) [A] The DNA delivery system according to Claim [37] 36 wherein the carrier is a targeted non-viral vector.

39. (amended) [A] The DNA delivery system according to Claim [38] 11 wherein [the targeted vector] the carrier is an antibody targeted liposome.

40. (amended) [A] The DNA delivery system according to Claim [38] 11 wherein [the targeted vector] the carrier is an antibody targeted condensed DNA.

41. (amended) [A] The DNA delivery system according to Claim [40] 11 wherein [the targeted vector] the carrier is an antibody targeted protamine or polylysine condensed DNA.

15 42. (amended) [A] The DNA delivery system according to Claim [38] 11
wherein [the targeted vector] the carrier is antibody targeted naked DNA.

346 46. (amended) An effector cell [according to Claim 45 which is] selected
from a lymphocyte, a dendritic cell, a B-cell, a haematopoietic stem cell, a
macrophage, a monocyte or a NK cell, transfected with a DNA delivery system
comprising DNA in association with a carrier said DNA coding for a recombinant
chimeric receptor capable of one type of extracellular interaction and wherein said
DNA codes in reading frame for:
i) a signal peptide component;
ii) an antibody or antigen binding fragment thereof;
iii) a transmembrane component;
iv) two or more different cytoplasmic signalling components which are not
naturally linked, and wherein at least one of said cytoplasmic components is derived
from a membrane spanning polypeptide; and optionally
v) one or more spacer regions linking any two or more of said i) to iv)
components.

47. An effector cell according to Claim 46 which is a cytotoxic T-lymphocyte.

50. (amended) A pharmaceutical composition comprising a DNA delivery
system [according to any one of Claims 11 to 44 together with one or more formulatory
agents] comprising DNA in association with a carrier said DNA coding for a
recombinant chimeric receptor capable of one type of extracellular interaction and
which said DNA codes in reading frame for:

i) a signal peptide component;
ii) an antibody or antigen binding fragment thereof;
iii) a transmembrane component;
iv) two or more different cytoplasmic signalling components which are not
naturally linked, and wherein at least one of said cytoplasmic components is derived
from a membrane spanning polypeptide; and optionally